syndrome in extensive haemangioma of the tongue and lip in a newborn infant.[4]

Thirdly, the substernal goitres reported in the literature have not been uniformly defined in relation to the proportion of the thyroid gland within the thorax. Therefore, it is rather difficult to compare the sizes and the results of reported series of substernal goitres. For the last decade, we and others[5] have chosen to refer to any goitre in which more than 50% of its mass is inferior to the thoracic inlet as substernal.

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## Anaphylactoid reaction to hydroxycobalamin with tolerance of cyanocobalamin

*Sir,*

A patient with an anaphylactoid reaction to hydroxycobalamin but good tolerance of cyanocobalamin is described, which emphasizes the usefulness of challenge tests in cases of allergic or pseudoallergic reactions.

A 33-year-old woman with a history of Crohn's disease developed subacute combined degeneration of the spinal cord due to vitamin B12 deficiency. Replacement therapy with hydroxycobalamin was established at a dose of 10 mg intramuscularly every month with no problems for more than a year. Unexpectedly, 2 hours after a dose, the patient developed generalised urticaria and angioedema with involvement of the upper airway. Prick and intradermal tests performed with 5 mg/ml and 100 μg/ml of hydroxycobalamin, respectively, were negative. Under in-hospital observation the patient was given 2500 μg of hydroxycobalamin by the intramuscular route; 20 min later, she experienced pruritus on her palms, shortly followed by generalised urticaria, prominent lip and palpebral oedema, hoarseness and chest tightness. The patient was treated with epinephrine, methylprednisolone and chlorpheniramine with total recovery in 2 hours. A challenge test with benzyl alcohol, added as preservative, was carried out with no reaction. On the basis that the neurologic manifestations would progress without adequate replacement treatment, a desensitisation protocol was developed. Increasing doses of hydroxycobalamin, beginning with 0.05 μg, were administered every 15 min by the intramuscular route. Ten minutes after the injection of 125 μg of hydroxycobalamin, the same allergic reaction appeared. Premedication with antihistamines did not provide reliably effective protection from the hydroxycobalamin-induced reaction in the patient. However, intramuscular challenge tests with cyanocobalamin up to 10 mg, performed on three different occasions, were followed by no reaction. At present, the patient receives 10 mg of cyanocobalamin monthly without problems.

Cobalamin is an organometallic vitamin which cannot be synthesized in the human body and must be supplied in the diet. The minimum daily requirement is about 2.5 μg. In patients with disease of the distal small intestine such as Crohn's disease, cobalamin deficiency may develop. In order to avoid clinical features of cobalamin deficiency, especially neurologic manifestations, replacement therapy is suggested. Because oral absorption is inadequate, replacement must be administered parenterally. The vitamin preparations which are used therapeutically are cyanocobalamin and hydroxycobalamin (both also called vitamin B12) given intramuscularly at monthly periods and maintained indefinitely. Allergic reactions to vitamin B12 are rare but can be observed even after several years of treatment.[1] James and Warin reported one patient with dyspnoea and urticaria in the course of a treatment with cyanocobalamin and hydroxycobalamin in which specific IgE could not be showed, suggesting an anaphylactoid reaction rather than a real allergic mechanism.[2] Recognising that a reaction is caused by direct histamine release may be important since treatment can generally be continued by lowering the dose of the drug. In the patient reported here, the immediate response obtained with low doses of hydroxycobalamin (125 μg) on rechallenge, the tolerance of previous doses of this drug (sensitisation period), together with the perfect tolerance of therapeutic doses of cyanocobalamin suggests an allergic mechanism even in the presence of negative skin tests. Even though the reaction developed only at or above a dose of 125 μg, it is difficult to explain this as an anaphylactoid mechanism, since the capacity of hydroxycobalamin and cyanocobalamin to induce direct release of histamine is quite similar. A reaction to an excipient rather than to the drug itself was ruled out because the only preservative in the formulation was benzyl alcohol (provided by the manufacturer) which was well tolerated by the patient on challenge. Up to now, positive skin tests with hydroxycobalamin have been described in only two patients.[3-4] Accordingly, cyanocobalamin may be tried as an alternative in patients with a history of systemic reactions to hydroxycobalamin.

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## Salvage angioplasty following failed thrombolysis

*Sir,*

Drs Mahy and Jennings are correct to point out the dilemmas facing physicians responsible for the further management of patients with acute myocardial infarction and apparent failure to respond to thrombolytic therapy.[1] The lack of evidence supporting any particular management strategy is surprising given that up to 50% of patients fail to respond to thrombolytic therapy in the first few hours and that persistent ST segment elevation following acute myocardial infarction (AMI) is clearly associated with poor outcome. Purcell *et al*[2] demonstrated a mortality of 18.2% in unselected patients with AMI and <50% resolution of ST segment elevation in the worst lead 60 minutes after the initiation of thrombolytic therapy. A substudy[3] of the INJECT trial revealed a mortality of 17.5% in patients with ≤30% resolution of the summed ST segment elevation in leads reflecting the infarct zone. Even though it is frequently stated that such electrocardiographic (ECG) features are not 100% sensitive or specific for persistent arterial occlusion, the presence of such features must alert us to a patient who is at high risk of further adverse events. Salvage angioplasty has only been examined in one large prospective randomised study against conservative therapy.[4] Despite a statistically significant reduction in the incidence of death or severe heart failure, this strategy has not been widely adopted nor examined further in the modern angioplasty era. This is surprising, given that this study probably *underestimated* the benefit of salvage angioplasty for a number of reasons. Firstly, high-risk patients, including those with a previous myocardial infarction who are perhaps more likely to benefit from attempts to open a second vessel, were excluded. Secondly, patients in this trial were taken on for salvage angioplasty relatively late after the onset of chest pain. Thirdly, intra-aortic balloon counterpulsation was rarely used, but is now known to reduce the risk of arterial occlusion following salvage angioplasty.[5] Fourthly, the trial was performed without modern glycoprotein IIb/IIIa inhibitors, such as abciximab (Reopro®). These agents have been shown to be beneficial in high-risk angioplasty without increased risk of haemorrhage.[6] Lastly, and most importantly, this trial was performed in the early 1990s before the modern coronary artery stent era. It is undoubtedly the case that the availability of coronary artery stents allows angioplasty in the context of AMI to be performed with greater success. We would go so far as to say that the results of the trials of immediate angioplasty following thrombolytic therapy, which universally demonstrated unfavourable outcomes with this strategy, have no relevance in the modern stent era. This is an area which commands further study. Our policy of performing salvage angioplasty in the context of <50% ST segment resolution in the worst lead 2 hours after the initiation of thrombolytic therapy has produced favourable results, especially if the patient presents promptly, receives thrombolysis promptly and the 2-hour ECG is scrupulously reviewed. Our experience is that this policy can reduce mortality from an expected 17–20% to 5%. Thus, patients with persistent ST elevation following thrombolytic therapy should be considered early for